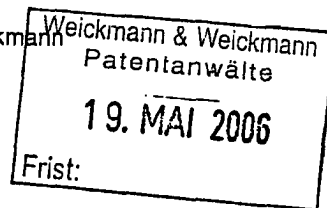


**PCT**

NOTIFICATION OF TRANSMITTAL  
OF COPIES OF TRANSLATION  
OF THE INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY  
(CHAPTER I OR CHAPTER II  
OF THE PATENT COOPERATION TREATY)  
(PCT Rules 44bis.3(c) and 72.2)

To:

DEY, Michael  
Weickmann & Weickmann  
Postfach 860 820  
81635 München  
ALLEMAGNE



Date of mailing (day/month/year) 11 May 2006 (11.05.2006)	
Applicant's or agent's file reference 33132P WO	<b>IMPORTANT NOTIFICATION</b>
International application No. PCT/EP2004/006320	International filing date (day/month/year) 11 June 2004 (11.06.2004)
Applicant MEDICAL ENZYMES AG et al	

## 1. Transmittal of the translation to the applicant.



The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).



The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

## 2. Transmittal of the copy of the translation to the designated or elected Offices.

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

None

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EG, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

## 3. Reminder regarding translation into (one of) the official language(s) of the elected Office(s).

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Authorized officer

Ellen Moyse

## PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY  
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 33132P WO	<b>FOR FURTHER ACTION</b>		See item 4 below
International application No. PCT/EP2004/006320	International filing date ( <i>day/month/year</i> ) 11 June 2004 (11.06.2004)	Priority date ( <i>day/month/year</i> ) 11 June 2003 (11.06.2003)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant MEDICAL ENZYMES AG			

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- |  |   |
|--|---|
| <input checked="" type="checkbox"/> Box No. I  | Basis of the report   |
| <input checked="" type="checkbox"/> Box No. II | Priority  |
| <input type="checkbox"/> Box No. III           | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability  |
| <input type="checkbox"/> Box No. IV            | Lack of unity of invention  |
| <input checked="" type="checkbox"/> Box No. V  | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> Box No. VI            | Certain documents cited   |
| <input type="checkbox"/> Box No. VII           | Certain defects in the international application  |
| <input type="checkbox"/> Box No. VIII          | Certain observations on the international application   |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Date of issuance of this report 01 May 2006 (01.05.2006)
	Authorized officer  Ellen Moyse
Facsimile No. +41 22 740 14 35	Telephone No. +41 22 338 89 75

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

# PCT

**Translation**

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:

Date of mailing  
(day/month/year)

Applicant's or agent's file reference

**33132P WO**

**FOR FURTHER ACTION**

See paragraph 2 below

International application No.

**PCT/EP2004/006320**

International filing date (day/month/year)

**11.06.2004**

Priority date (day/month/year)

**11.06.2003**

International Patent Classification (IPC) or both national classification and IPC

Applicant

**MEDICAL ENZYMES AG**

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/EP

Authorized officer

Facsimile No.

Telephone No.

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2004/006320

Box No. 1 Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐

This opinion has been established on the basis of a translation from the original language into the following language

\_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐

a sequence listing

☐

table(s) related to the sequence listing

b. format of material

☐

in written format

☐

in computer readable form

c. time of filing/furnishing

☐

contained in the international application as filed.

☐

filed together with the international application in computer readable form.

☐

furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2004/006320

Box No. II

Priority

1. ☒ The following document has not yet been furnished:

☒ copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2004/006320

Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement		
1. Statement			
Novelty (N)	Claims	1-9	YES
	Claims		NO
Inventive step (IS)	Claims	1-9	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-9 (see text)	YES
	Claims		NO
2. Citations and explanations:			
<p>1. The application states that an unexpected synergistic effect exists for the combination of glutaminase with antineoplastic anthracyclines or platinum complexes.</p> <p>When there is a synergistic effect, the combination of drugs (A + B) has a superadditive effect compared with the purely computational combination of the effects of A plus B; e.g. effect of A = 20% and of B = 30%, whereas the combination (the combination product) (A + B) yields an effect of 80%.</p> <p>It must be taken into account in the interpretation of the data according to the figures that the growth is indicated therein in %. The effect achieved by the drugs must therefore be calculated using (100 - %).</p> <p>2. Hence, the effects (= growth inhibition) of the drugs emerge for <b>mitomycin</b> and CNS SF-539 cells (fig. 1) as being:</p> <p>glutaminase (100-21) = 79%</p> <p>mitomycin (100-99) = 1%</p>			

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/EP2004/006320

Box No. V

Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement

total = 80%

(glutaminase + mitomycin) = (100 - 7) = 93%

Comparison of the total (80%) with the actually achieved combination effect (97%) shows that a synergistic effect is present in this case.

The same is true approximately for **mitoxanthrone** on breast MCF7 cells according to fig. 2 and for **cis-platin** on MCF7 cells according to fig. 3.

3. Since there appears to be no relevant prior art, the subject matter of claims 1-9 is regarded as novel and inventive.
4. The description should be made consistent with the claims. Accordingly, only the chemotherapeutic agents mentioned in the claims as agents suitable for combination products should remain in the description. There is no evidence of a synergistic effect for any chemotherapeutic agents other than those mentioned in the claims.
5. The PCT Contracting States do not have uniform criteria for assessing the industrial applicability of claim 9 in its present form. Patentability may also depend on the wording of the claims. The EPO, for example, does not recognize the industrial applicability of claims to the medical use of a compound; it may, however, allow claims to the first medical application of a known compound or to the use of such a compound in the manufacture of a drug for a new medical application.